

in these fringe areas don't even have clean drinking water.

"The mismanagement of the urban fringe is becoming an increasing threat to the health and wellbeing of both urban and peri-urban citizens. But opportunities for a more positive relationship between the city and its periphery do exist and should be urgently addressed at Rio+20 and beyond," Marshall and Mehta conclude.

Fred Pearce, author of the recently published book *The Landgrabbers*, pointed to another "glaring hole" in the Rio+20 agenda: land rights. Pearce observes that "unprecedented corporate privatisation and enclosure of the world's common lands — its pastures, fields and forests — is being done in the name of development". However, he objects that "much of it will destroy development and impoverish the poorest".

There is certainly no shortage of problems to be discussed at Rio, but the question is whether the meeting can come up with constructive answers and solutions that will be implemented in the real world. Sustainable Development Goals (SDGs) as successors to the Millennium Development Goals may be one palpable outcome of it.

And then there is the small question of who will show up for the meeting. Newly elected presidents François Hollande and Vladimir Putin have confirmed their participation, while David Cameron and Angela Merkel are going to stay away. At the time of going to press it appeared unlikely that US president Obama will find the time to fly to Rio after the G20 meeting in Cabo San Lucas, Mexico. He may be too busy campaigning for the upcoming election. And the fact that attending Rio and helping to create a better future for the whole world wouldn't help Obama win favours with the undecided voters back home is in itself a clue to where we may find the stumbling blocks on the path to sustainable development.

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Q & A

György Kemenes

György (aka George) Kemenes is Professor of Neuroscience at the University of Sussex. He studied Biology at Eötvös Loránd University (ELTE), Budapest. He completed a PhD in Neurobiology (awarded by ELTE in 1985) under János Salánki's guidance at the Biological Research Institute of the Hungarian Academy of Sciences (HAS) in Tihany, where he then started working in a permanent research position. While still doing his research in Hungary, he was awarded several prestigious international visiting fellowships, which he spent working with Paul Benjamin in the UK and David Carpenter in the US. In 1990 he moved to York to work with Chris Elliott on a two-year research project. In 1992, he was invited to join the Sussex Centre for Neuroscience, a newly established Interdisciplinary Research Centre (IRC), funded by the UK Biology and Biotechnology Research Council (BBSRC). In 1996 he was conferred the DSc title by HAS and became a UK-based Scientific Advisor to the Tihany Biological Research Institute. In 1999 he was awarded an MRC Senior Non-clinical Fellowship at Sussex, followed by a five-year MRC Research Grant in 2005. He became Professor of Neuroscience in 2005. His research has been dedicated to understanding how even seemingly simple nervous systems can generate complex forms of behaviour, including associative learning, and how defined invertebrate neural circuits can be used to study evolutionarily conserved cellular and molecular mechanisms of memory function and dysfunction. He is a Fellow of the Society of Biology and a member of the editorial board of Neural Systems & Circuits.

What turned you on to biology in the first place? I was turned on to biology while still at primary school; however, it was not the influence of a good teacher, but simply fierce teenage competition with a classmate of mine that steered me in the direction of biology. We were about 13 and we tried to beat each other at everything we did, from

playing sports, through drawing horror comics (which we mainly did during lessons), to getting the attention of the prettiest girls in the class. He by then had developed a genuine strong interest in biology and decided to enter the annual Biology Challenge competition organized by the local education authority for primary school children. Naturally, I also decided to enter the same competition just to try to beat him. He won the whole competition — I had no chance against him, or indeed against many of the other kids who also competed — but while I was preparing for this competition I got hooked on biology, particularly animal behaviour. And it is just as well he did not become a biologist himself — otherwise he might be writing this Q & A instead of me!

Do you have a favourite paper? I don't have a 'favourite' paper as such, but I have very vivid memories of reading some fantastic papers presenting findings and ideas that were a real revelation to me at the time and actually had a major influence on my career. Perhaps unusually, however, the two papers that were most inspirational for me were not primary research papers but excellent reviews of findings from two then emerging areas in learning and memory research. The first of these papers was Tom Carew's 1996 *Neuron* review "Molecular enhancement of memory formation", an excellent overview of the rapidly expanding field of the role of transcriptional mechanisms in synaptic plasticity and learning and memory. It was this review that made me embark on investigating the possible role of cAMP Element Binding Protein (CREB) in the formation of 'flash-bulb'-like long-term associative memory in *Lymnaea stagnalis*. By 1996 I had been using this molluscan species in my experiments on behavioural and electrophysiological aspects of learning and memory for over a decade, and from then onwards I successfully expanded my research in the direction of top-down analysis of the molecular mechanisms of learning and memory using *Lymnaea* as my model. This research was funded for over 10 years by the MRC and BBSRC and has resulted in the publication of 19 primary research

papers since 2000 — all this initially triggered by the thoughts and ideas I formulated after reading that 1996 review.

The second review that had a great intellectual impact on me was Yadin Dudai and Mark Eisenberg's 2004 *Neuron* review "Rites of passage of the engram: reconsolidation and the lingering consolidation hypothesis". At the time there was a hot debate over the old and controversial idea of memory reconsolidation, rekindled by the publication in 2000 of the *Nature* paper "Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval" by Karim Nader, who was then working with Joseph LeDoux. But what really fascinated me was the hypothesis of 'lingering memory consolidation'. According to this hypothesis, even seemingly fully consolidated long-term memories may undergo further changes driven by molecular mechanisms that can become spontaneously active in certain time windows but also can be activated by the retrieval of the memory trace. Thus, the 2004 *Neuron* review proposed that reconsolidation was a manifestation of lingering consolidation rather than a recapitulation of consolidation. Since then, in our top-down experiments with *Lymnaea*, not only have we shown that specific signalling molecules are activated differentially during the retrieval of shorter and longer-term memories, but we have also found solid evidence to support the 'lingering consolidation' hypothesis and established the roles specific signalling kinase enzymes, such as PKA and CaMKII, play in it.

What is the best advice you have been given? The best advice I have ever been given concerning my career in biology actually came from my father, although he was not a biologist himself but a well-known economist. Sadly, he died in 2003 and so did not live to see me promoted to a Chair in Neuroscience, which would have made him immensely proud of me. When my first application for admission to study biology at ELTE was rejected despite my excellent matriculation grades, I was desolate and was fully resigned to the fact that I might never become a biologist. But my father gave me the advice to apply again in the following year.

He knew — but did not tell me at the time — that my rejection had little to do with my grades. The main reason was that I was a pupil of the Budapest Piarist Secondary School (Piarists is the name of the oldest Catholic educational order). This famous school, also attended by my father and his father before him, was established in 1717 and was one of only eight Catholic schools in Hungary that were not banned by the Communist regime in 1950. In the 1970s, however, there was still an unwritten rule according to which most pupils from religious schools were denied entry to university when they applied for admission right after finishing school and without first cutting their teeth at manual labour. So I followed my father's advice and went to work in a factory for a year and was admitted to study Biology at ELTE on my second attempt. But even this was a deferred admission, as at the time all young men admitted to university had to serve 11 months in Hungary's conscript army before starting their university education. So by the time I actually started studying for my Biology degree I had come to fully appreciate my status as a university student.

What advice would you offer someone wondering whether to start a career in biology? The advice I would offer is this: if you feel that biology is really what you want to do, go for it and persevere when initially things don't turn out to be as you hoped. Take good advice that helps you achieve this goal and never listen to anybody who tries to talk you out of pursuing an academic career in biology!

How did you end up working in the United Kingdom rather than in Hungary, which is particularly famous for its neuroscience research? This is a difficult question to answer. I had never originally planned to stay in the UK beyond the two years I spent in York between 1990 and 1992. But then I joined the Sussex Centre for Neuroscience, where we had continuous funding until 1999. During this period, the IRC (directed by Michael O'Shea) was the top centre in the whole of Europe, if not the whole world, for work in the field of invertebrate neuroscience, so I kept postponing my return to

Hungary (even though my old institute actually kept my permanent position open for me until 1999, in case I decided to return to Hungary). In 1998 my wife, Ildikó also started working full-time in neuroscience research at Sussex, after giving up a permanent job at Budapest Zoo, so the die was cast. Then, in 1999, I was awarded my first totally independent large UK grant, which was followed by other large grants in 2003 and 2005 and the promotion to Chair in 2005 — and the rest is history.

I have, however, always maintained very strong links with Hungarian academia and research. I set up ERASMUS teacher exchange programmes with ELTE and the University of Debrecen, where I taught several courses, and I also taught a number of courses at Szeged University. Over the years, many a young Hungarian scientist has come to work in my lab for shorter or longer periods and co-authored papers with me (amongst them a paper published in *Current Biology* in 2008). Several senior Hungarian neuroscientists have also come to give talks at our long-running Sussex Neuroscience Seminar series.

Were there any other factors outside your academic activities that helped your professional development? Yes, and they came from a rather unusual direction for a scientist. Shortly after joining the Tihany institute to start my research career, I took up Shotokan Karate, a very traditional and disciplined form of Japanese martial art. I practised this for more than 15 years in Hungary, in the States and of course in the UK, and it helped me enormously in becoming very focused in everything I did, including my research. And this extremely physical activity was a perfect complement to my sedentary lifestyle as a lab-based researcher. These days I no longer practise Shotokan but nearly seven years ago now I took up traditional Tai Chi, which is not as explosively physical as karate but helps even more in concentrating the mind on the task at hand, be it writing a paper or a grant or teaching a lecture. Everyone in academia should learn the Tai Chi exercise known as 'Calming the Mind', it works wonders when you get a paper rejected or a grant turned down!

What are you focusing on at the moment? I am still carrying on with my research into the molecular mechanisms of memory, currently focusing on the link between CaMKII and AMPA receptors during memory consolidation. But two years ago, funded by the BBSRC, we embarked on an exciting new project, investigating the link between decision-making and learning in *Lymnaea*. This project uses much less molecular analysis than my previous projects, instead relying on some powerful new neurophysiological methods, such as multi-electrode array (MEA) recording and dynamic clamp as well as classical intracellular microelectrophysiology, a technique I first learned when I was still working on my PhD project in Hungary. The big scientific question we are focusing on at the moment is how such complex behavioural phenomena as decision-making are generated at the level of precisely defined and interacting neural networks and how they are shaped by learning.

What is your opinion concerning the future of invertebrate model systems in neuroscience research? Some years ago a certain 'gloom-and-doom' sentiment started spreading in the invertebrate neuroscience community concerning the future of the use of invertebrate model organisms in biomedical research. Undoubtedly, it is much harder to get neuroscience research on invertebrate animals funded than it was say 10 years ago. However, to a large extent this is also true for research using vertebrate models. I still believe that, at least in the UK, research based on exciting new ideas and using powerful new tools to address still unresolved questions of general biological importance still has a good chance of being funded, whatever the model system. I am convinced that research using invertebrates will continue to make a significant contribution to our understanding of the most fundamental and evolutionarily conserved principles of nervous system function and dysfunction.

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Quick guide

Entomopathogenic nematodes

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What are entomopathogenic nematodes? Nematodes seem to have evolved to occupy nearly every niche imaginable, including a wide diversity of parasitic niches. Among the vast variety of parasitic nematodes, some have evolved an association with insect-pathogenic bacteria. Together the bacteria and nematode are a lethal duo. These nematodes are called 'entomopathogenic nematodes'. Essentially the nematodes serve as mobile vectors for their insect-pathogenic bacteria cargo, like little Typhoid Marys. The nematodes seek out and invade potential hosts and release their pathogenic payload into the nutrient-rich hemolymph. Infected insect hosts die quickly, the bacteria proliferate, the nematodes feed on bacteria and insect tissues, and reproduce. When the host cadaver is depleted of resources, nematodes associated with pathogenic bacteria emerge and search for new hosts to infect (Figure 1). The cooperation with bacteria and the speed with which they kill set entomopathogenic nematodes apart from other nematode parasites.

How do they kill? The nematode and its pathogenic bacteria cargo contribute to varying degrees, depending on the specific combination. The known bacterial associates of entomopathogenic nematodes, *Photorhabdus* and *Xenorhabdus* species, are known to produce a toxic cocktail of secondary metabolites that not only are lethal to the insect hosts, but also prevent opportunistic bacteria and fungi from utilizing the nutrient-rich cadaver, sequestering the resources for themselves and their nematode partners. The bacteria always contribute to the virulence of the duo, and usually contribute the lion's share. Some species of nematodes are thought merely to shuttle the

bacteria, contributing very little to host death, while others are known to be lethal in their own right, producing a variety of secreted protein products that degrade and digest host tissues, in addition to short-circuiting the host immune system. Even though some nematodes appear lethal on their own, all entomopathogenic nematodes known are associated with bacteria.

Are all stages infectious? The short answer is no. Only a modified third larval stage called the infective juvenile, analogous to the dauer juvenile stage in *Caenorhabditis elegans*, is infectious. In fact, infective juveniles are the only free-living stage of known entomopathogenic nematodes, while all other developmental stages are only found inside infected hosts. The infective juvenile is a stress-tolerant, non-feeding, bacterial-vectoring stage that seeks out insects to infect and kill.

How did they get their name? The first entomopathogenic nematode was described by Gotthold Steiner in 1923; since then more than 75 species have been described, with more species being described every year. Most studies focus on entomopathogenic nematodes from two genera: *Steinernema* and *Heterorhabditis*. It is through their association with insect-pathogenic bacteria that they began to be called entomopathogenic nematodes. First the nematodes' bacterial partners were called entomopathogenic bacteria because these bacteria have a median lethal dose or LD₅₀ of 10,000 cells or less. This means that an inoculum of 10,000 bacterial cells or less, into the hemolymph, kills half of a tested population of insects. The term 'entomopathogenic' began to be applied to the nematodes themselves in the late 1980s and reinforces the link between nematology and insect pathology. It is a useful technical epithet that differentiates them from other types of parasitic nematodes, of which there are many.

Are they harmful to humans? While most parasitic nematodes might be seen as harmful, entomopathogenic nematodes are beneficial to humans. Their potential as alternatives to chemical pesticides for controlling pesky insects was recognized early